* * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

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=> file reg

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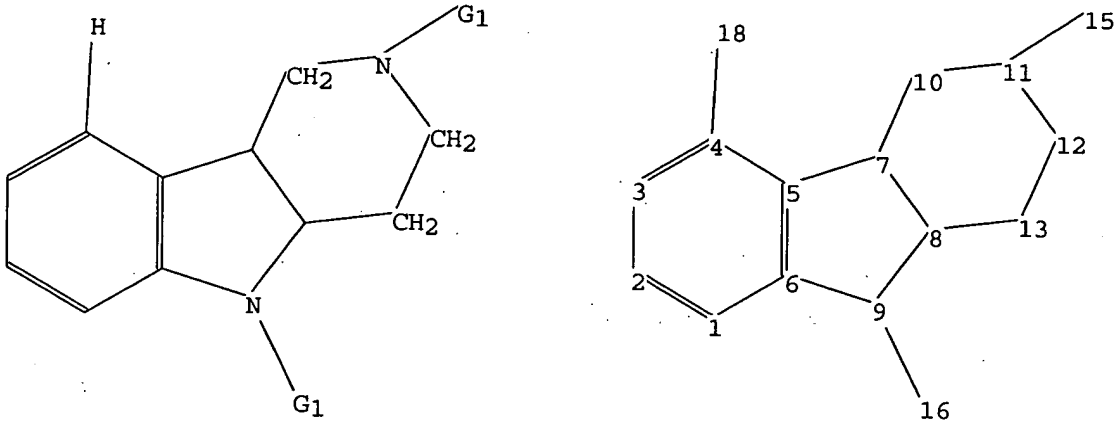


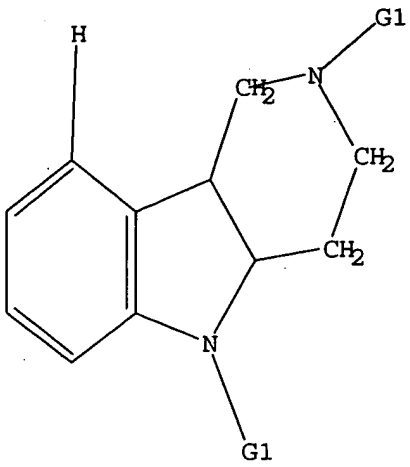
chain nodes :
15 16 18
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13
chain bonds :
4-18 9-16 11-15
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 7-10 8-9 8-13 10-11 11-12 12-13
exact/norm bonds :
6-9 8-9 9-16 11-15
exact bonds :
4-18 5-7 7-8 7-10 8-13 10-11 11-12 12-13
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G1:C,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 15:CLASS 16:CLASS 18:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 C,H

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 full
L3          1026 SEA SSS FUL L1

=> file ca

=> s l3
L4           315 L3

=> s 5ht
L5          2702 5HT

=> s l4 and l5
L6             1 L4 AND L5

=> s l4 and (pharm? or drug?)
         517571 PHARM?
         719946 DRUG?
L7           149 L4 AND (PHARM? OR DRUG?)

=> s l6 or l7
L8           150 L6 OR L7

=> d l6 ibib abs fhitstr
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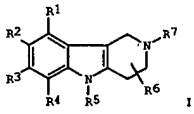
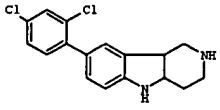
L6 ANSWER 1 OF 1 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:170224 CA
TITLE: Preparation of 1H-pyrido[4,3-b]indoles as 5-HT receptor ligands
INVENTOR(S): Ennis, Michael D.; Frank, Kristine E.; Hoffman, Robert L.; Fu, Jian-Min
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014118	A1	20030220	WO 2002-US25130	20020806
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2453537	AA	20030220	CA 2002-2453537	20020806
US 2003060464	A1	20030327	US 2002-214405	20020806
US 6849640	B2	20050201		
EP 1414819	A1	20040506	EP 2002-757023	20020806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-310890P P 20010808
WO 2002-US25130 W 20020806
OTHER SOURCE(S): MARPAT 138:170224
GI

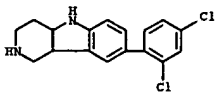

I


II

AB 2,3,4,4A,5,9b-hexahydro-1H-pyrido[4,3-b]indoles and 2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indoles of formula I [R1-R4 = H, halo, CF3, OCF3, CN, NO2, alkyl, cycloalkyl, (substituted) OH, aryl, etc.; R5 = H, alkyl, cycloalkyl, aryl, heteroaryl, etc.; R6 = H, alkyl; R7 = H, alkyl, alkenyl, alkynyl, aryl, etc.]; are prepd. These compds. are 5-HT ligands that are useful for treating diseases wherein modulation of 5-HT activity is desired. Thus, II was prepd. from 8-bromo-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole and 2,4-dichlorophenyl boronic acid in 4 steps. The compds. displace >50% of a radiolabeled test ligand from 5-HT receptor subtypes at 1 μM concn.

IT 497261-07-1P
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridoindoles as 5-HT receptor ligands)

RN 497261-07-1 CA
CN 1H-Pyrido[4,3-b]indole, 8-(2,4-dichlorophenyl)-2,3,4,4a,5,9b-hexahydro-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/743,449

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=> s l7 and py<2003
      21763362 PY<2003
L9          134 L7 AND PY<2003

=> d ibib abs fhitstr 1-50
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L9 ANSWER 1 OF 134 CA COPYRIGHT 2005 ACS on STN

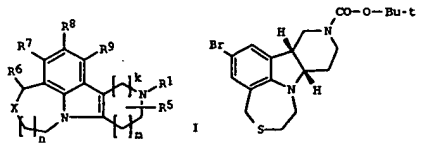
ACCESSION NUMBER: 137:140432 CA
TITLE: Preparation of pyridoindoles as human serotonin receptor 5-HT2C agonists and 5-HT2A antagonists
INVENTOR(S): Robichaud, Albert J.; Fevig, John M.; Mitchell, Ian S.; Lee, Taekyu; Chen, Wenting; Cacciola, Joseph
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 409 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059129	A2	20020801	WO 2001-US49371	20011219 <--
WO 2002059129	A3	20030130		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432185	AA	20020801	CA 2001-2432185	20011219 <--
EP 1343791	A2	20030917	EP 2001-994316	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300296	A	20031215	EE 2003-296	20011219
JP 2005506281	T2	20050303	JP 2002-559431	20011219
BG 107865	A	20040730	BG 2003-107865	20030530
ZA 2003004305	A	20040902	ZA 2003-4305	20030602
NO 2003002797	A	20030819	NO 2003-2797	20030619

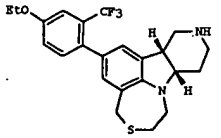
PRIORITY APPLN. INFO.: US 2000-256740P P 20001220
WO 2001-US49371 W 20011219

OTHER SOURCE(S): MARPAT 137:140432
GI

L9 ANSWER 1 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



I II



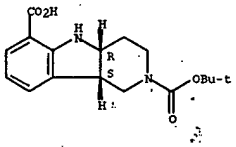
II

AB Title compds. I and their pharmaceutically acceptable salts [R1 = H, alkyl, alkenyl, alkynyl, etc.; R5, R6 = H, alkyl; R7, R8, R9 = H, halo, CF3, aryl etc.; k, n = 1, 2; m = 0, 1; X = O, S, SO, etc.] and formulations were prepared For example, Suzuki coupling of chiral bromide II, e.g., prepared in 7 steps from 1,5-dihydro-4,1-benzothiazepin-2(3H)-one, and 4-ethoxy-2-trifluoromethylphenyl boronic acid, followed by BOC deprotection afforded pyridothiazepinoindole.TFA III. In vitro radioligand binding assays, compds. I had IC50 values < 50 μM for 5-HT2A antagonism or 5-HT2C agonism. Compds. I are useful in the control or prevention of central nervous system, sexual, gastrointestinal disorders etc..

IT 444721-89-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyridoindoles as human serotonin receptor 5-HT2C agonists and 5-HT2A antagonists)

RN 444721-89-5 CA
CN 2H-Pyrido[4,3-b]indole-2,6-dicarboxylic acid, 1,3,4,4a,5,9b-hexahydro-, 2-(1,1-dimethylethyl) ester, (4aR,9bS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L9 ANSWER 1 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

L9 ANSWER 2 OF 134 CA COPYRIGHT 2005 ACS on STN

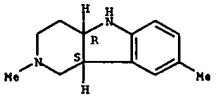
ACCESSION NUMBER: 135:267165 CA
TITLE: Stobadine protects isoproterenol-induced toxic damage in rats
AUTHOR(S): Macickova, Tatiana; Navarova, Jana
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-84216, Slovakia
SOURCE: Biologia (Bratislava) (2000), 55(Suppl. 8), 69-73
CODEN: BLOAAO; ISSN: 0006-3088
PUBLISHER: Slovak Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pyridoindole stobadine (STO) is an effective cardioprotective drug with oxygen free radical scavenging properties. Isoproterenol (IPN), a synthetic catecholamine, is capable to induce massive myocardial necrosis accompanied with lysosomal enzyme (LE) activity changes in most mammals, when administered in high doses. The present study investigated the ability of STO to protect exptl. animals against IPN-induced toxic damage. The activities of the lysosomal enzymes cathepsin D and N-acetyl-β-D-glucosaminidase were studied in the rat heart as markers of cell damage. Male Wistar rats weighing 280-300g were used for these expts. IPN-induced toxic damage in rats (9 h after mg.kg-1 s.c.) was manifested by marked alterations in the activities of LE in the sedimentable fraction of the rat myocardium. STO administered in various dosage regimens reduced or eliminated the IPN-induced biochem. changes in the rat myocardium. From the results presented in this study we conclude that STO is able to protect rats against IPN-induced toxic damage.

IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stobadine protects against isoproterenol-induced toxic damage in rats)

RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

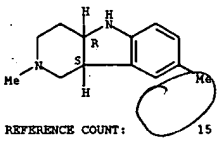
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:267164 CA
TITLE: Effects of stobadine on hypoxia and hypoxia/reoxygenation injury in isolated hepatocytes from fasted rats
AUTHOR(S): Bezek, Stefan; Juranek, Ivo
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-84216, Slovakia
SOURCE: Biologia (Bratislava) (2000), 55(Suppl. 8), 15-18
CODEN: BLOAAO; ISSN: 0006-3088
PUBLISHER: Slovak Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cell injury due to hypoxia and reoxygenation was investigated in the system of parenchymal hepatocytes isolated from fasted rats. The functional and structural integrity of hepatocytes in hypoxia was evaluated on the basis of protein synthesis and [86Rb] release from prelabeled hepatocytes. Incubation of hepatocytes in nitrogen atmospheric resulted in significant inhibition of incorporation of [14C]-valine into hepatocyte protein. Treatment of hepatocytes in hypoxia with the antioxidant stobadine (0.1, 1.0 and 10.0 μM) reversed protein synthesis almost to control values. No changes were observed in [86Rb] release from prelabeled hepatocytes. In the experiment with hypoxia/reoxygenation, hepatocytes were exposed to 60 min hypoxia followed by 120 min reoxygenation and the injury was evaluated by lactate dehydrogenase (LD) leakage and formation of thiobarbituric acid reactive substances (TBARS). The addition of stobadine at the given concns. (0.1, 1.0 and 10.0 μM) before the onset of hypoxia resulted in dose dependent protection from hypoxia/reoxygenation injury of isolated hepatocytes.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of stobadine on hypoxia and hypoxia/reoxygenation injury in isolated hepatocytes from fasted rats)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

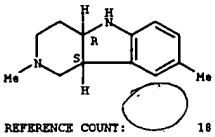
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:266992 CA
TITLE: Effect of stobadine on superoxide generation and degranulation of stimulated human polymorphonuclear leukocytes in vitro
AUTHOR(S): Pecivova, Jana; Macickova, Tatiana; Nosal, Rado; Danihelova, Edita
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-84216, Slovakia
SOURCE: Biologia (Bratislava) (2000), 55(Suppl. 8), 103-106
CODEN: BLOAAO; ISSN: 0006-3088
PUBLISHER: Slovak Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors studied the effect of stobadine, a pyridoindole antioxidant agent, on superoxide anion (O2.-) generation (respiratory burst) and enzyme (lysozyme and myeloperoxidase) release from FMLP (a specific receptor activator) and from PMA (activator of protein kinase C) stimulated human polymorphonuclear leukocytes (PMNL). Stobadine (1, 10, and 100 μM) decreased O2.- generation in FMLP stimulated PMNL only. It had no effect on enzyme release. The stobadine effect on O2.- generation seems to be linked to signal transduction rather than to its free radical scavenging and antioxidant properties since there was no effect on O2.- generation in PMA stimulated PMNL.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stobadine on superoxide generation and degranulation of stimulated human polymorphonuclear leukocytes in vitro)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

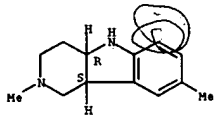
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:221089 CA
TITLE: Antiradical activity of some antiulcer and local anesthetic active substances
AUTHOR(S): Dovolil, J.; Benes, Ludek
CORPORATE SOURCE: Ustav Chem. Leciv, Farm. Fak., Vet. a Farm. Univ., Brno, 612 42, Czech Rep.
SOURCE: Ceska a Slovenska Farmacie (2001), 50(4), 203-205
CODEN: CSLFEK; ISSN: 1210-7816
PUBLISHER: Ceska Lekarska Spolecnost J. Ev. Purkyne
DOCUMENT TYPE: Journal
LANGUAGE: Czech
AB The in vitro free radical scavenging effects of 15 pharmacol. agents were examined by the the diphenyl-p-picrylhydrazyl assay (decrease in absorbance). Methylpentacainium iodide, mannitol, ascorbic acid, and HCl forms of pentacaine (K-1902), K-1904, K-1905, K-1906, K-1908, K-1909, K-1913, P-18, P-20, carbisocaine, lidocaine, stobadine were tested. A pronounced antiradical activity was observed with trapencaine, more than with stobadine, ascorbate, and mannitol. Trapencaine derivs. and lidocaine were less effective in comparison with trapencaine. The methylene group in the hydrophilic moiety of the trapencaine mol. (stereoisomers P-18 and P-20) led to the loss of antiradical activity, but the cis-isomer was more effective than the trans-isomer. The data suggest relationships of the chemical structure and antiradical and gastric cytoprotective activities.
IT 95751-51-2, Stobadine dihydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antiradical activity of 15 antiulcer and local anesthetic agents in vitro)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

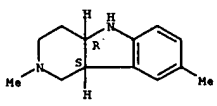
Absolute stereochemistry. Rotation (-).



●2 HCl

L9 ANSWER 6 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:189681 CA
TITLE: Placental transfer of the antioxidant stobadine at different gestational stages in rabbits
AUTHOR(S): Ujhazy, E.; Dubovicky, M.; Faberova, V.; Zemanek, M.; Soltes, L.; Gajdosik, A.; Eybl, V.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (2000), 22(9), 683-688
CODEN: MFEPDX; ISSN: 0379-0355
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The distribution of [3H]-stobadine, a pyridoindole antioxidant, was investigated in New Zealand white rabbits and their fetuses on days 20 and 27 of gestation. The concns. of [3H]-stobadine were determined in maternal and fetal organs after oral administration in a single dose of 5.0 mg/kg. The results of the study showed that during the late period of gestation the fetal organs, especially the brain and heart, were under the protective action of the antioxidant stobadine.
IT 85202-17-1, Stobadine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(placental transfer of antioxidant stobadine at different gestational stages in rabbits)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 134 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 135:61175 CA
TITLE: Study of the kinetics of hydrolysis of stobadine acyl derivatives, the prodrug forms of extinguishers of free oxygen radicals. Part 3. Hydrolysis in neutral medium
AUTHOR(S): Ondrasova, Miriam; Stankovicova, M.; Bezakova, Z.; Benes, L.
CORPORATE SOURCE: Katedra Farm. Chem., Farm. Fak., Univ. Komenskeho, Bratislava, 832 32, Slovakia
SOURCE: Ceska a Slovenska Farmacie (2001), 50(2), 86-91
CODEN: CSLFEK; ISSN: 1210-7816
PUBLISHER: Ceska Lekarska Spolecnost J. Ev. Purkyne
DOCUMENT TYPE: Journal
LANGUAGE: Slovak

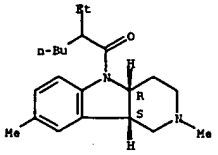
AB The pyridoindole derivative stobadine, [(-)-cis-2,8-dimethyl-2,3,4,4a,5,9b-hexahydro-1H-pyrido[4,3b]-indole] is a perspective antiarrhythmic, antihistamine, anesthetic, antiulcerous drug capable of extinguishing free oxygen radical. Its prodrug forms-N(5)-acyl-substituted stobadine - of the active substance - stobadine - have been prepared and it is assumed that the will be hydrolyzed in the organism and the active substance will be released in higher concns. in different biol. tissues. The present paper is concerned with the investigation of the kinetics of the hydrolysis of 13 acyl derivs. of stobadine in the medium of a buffer solution of pH 7 at temps. of 70°C and 75°C spectrophotometrically in the UV region of the spectrum. The determined rate consts. were correlated with the length of the side acyl chain and the pKa values of the drugs under study. The profile of log k-pH of substances was determined

IT 154853-56-2
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(kinetics of hydrolysis of stobadine acyl derivs., the prodrug forms of extinguishers of free oxygen radicals)

RN 154853-56-2 CA
CN 1H-Pyrido[4,3-b]indole, 5-(2-ethyl-1-oxohexyl)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, monohydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 7 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



● HCl

L9 ANSWER 8 OF 134 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 134:352757 CA
TITLE: Effect of dietary supplementation with the pyridoindole antioxidant stobadine on antioxidant state and ultrastructure of diabetic rat myocardium
AUTHOR(S): Stefek, M.; Sotnikova, R.; Okruhlicova, L.; Volkovova, K.; Kucharska, J.; Gajdosik, A.; Gajdosikova, A.; Mihalova, D.; Hozova, R.; Tribulova, N.; Gvozdjakova, A.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia
SOURCE: Acta Diabetologica (2000), 37(3), 111-117
CODEN: ACDAEZ; ISSN: 0940-5429
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

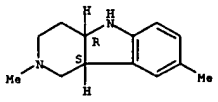
AB Consistent with the postulated role of oxidative stress in the etiol. of late diabetic complications, pharmacol. interventions based on biol. antioxidants have been suggested. The aim of the present study was to investigate the effect of dietary supplementation with the pyridoindole antioxidant stobadine on the myocardial antioxidant status and ultrastructure of streptozotocin-diabetic rats. Diabetic male Wistar rats were fed for 32 wk a standard diet or a diet supplemented with stobadine (0.05% weight/weight). Control rats received a standard diet or stobadine-supplemented diet (0.16% weight/weight). Plasma levels of glucose, cholesterol and triglycerides were increased significantly by diabetes. Activities of superoxide dismutase and catalase were markedly elevated in the diabetic myocardium. Myocardial levels of conjugated dienes increased after eight months of diabetes, in spite of significantly increased myocardial α-tocopherol and coenzyme Q9 content. The long-term treatment of diabetic animals with stobadine (i) reduced plasma cholesterol and triglyceride levels yet left the severe hyperglycemia unaffected, (ii) reduced oxidative damage of myocardial tissue as measured by conjugated dienes, (iii) reversed myocardial levels of α-tocopherol and coenzyme Q9 to near control values, (iv) reduced elevated activity of superoxide dismutase in the diabetic myocardium, and (v) attenuated angiopathic and atherogenic processes in the myocardium as assessed by electron microscopy examination. These results are in accordance with the postulated prooxidant role of chronic hyperglycemia and provide further evidence that development of pathol. changes in diabetic myocardium is amenable to pharmacol. intervention by biol. antioxidants.

IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of stobadine supplementation on antioxidant state and ultrastructure of diabetic rat heart)

RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L9 ANSWER 8 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

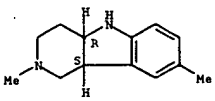
L9 ANSWER 9 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:336126 CA
TITLE: Preventive effect of several antioxidants after oxidative stress on rat brain homogenates
AUTHOR(S): Horakova, L.; Ondrejickova, O.; Bachrata, K.; Vajdova, M.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia
SOURCE: General Physiology and Biophysics (2000), 19(2), 195-205
CODEN: GPBIE2; ISSN: 0231-5882
PUBLISHER: Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Brain homogenate was used as a model system to study antioxidant properties of several natural and synthetic antioxidants under oxidative stress. Oxidative stress was induced by Fe/ascorbate system and lipid peroxidn. as well as protein modification were studied. Thiobarbituric acid reactive substances (TBARS) were used as a marker of lipid peroxidn. The preventive effect concerning lipid peroxidn. decreased in the order: butylated hydroxytoluene (BHT) (3.5), stobadine (ST) (35), serotonin (54), trolox (98), U 74389G (160), melatonin (3100), (the nos. in the brackets represent IC50 in μmol/l). Methylprednisolone had no effect, and spin traps interfered with TBARS determination Concerning creatine kinase (CK) activity as a selected marker of oxidative modification of proteins, the preventive effect of antioxidants (30 μmol/l) decreased in the order: BHT (30), trolox (75), stobadine (ST) (77), α-phenyl-N-tert-buthylnitrone (PBN) (87), sodium salt of N-tert-butyl-C-(phenyl-2-sulfone) nitrone (SPBN) (90), (the nos. in the brackets represent the loss of CK activity in percentages, when 100 % was the loss of CK activity in the absence of any antioxidant). The nonglucocorticoid steroid U 74389G, methylprednisolone, and serotonin had no preventive effects, while melatonin had antioxidant effect only in a higher concentration (1 mmol/l).

IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preventive effect of antioxidants after oxidative stress in brain)

RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



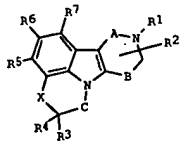
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

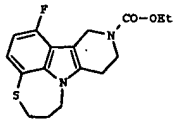
L9 ANSWER 10 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:56655 CA
TITLE: Preparation of substituted heterocycle fused gamma-carbolines
INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei; Mitchell, Ian S.; Yang, Michael Guang; Haydar, Simon; Chen, Wenting; McClung, Christopher D.; Calvello, Emilie J. B.; Zawrotny, David M.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 308 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077002	A1	20001221	WO 2000-US16498	20000615 <--
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2374239	AA	20001221	CA 2000-2374239	20000615 <--
EP 1189904	A1	20020327	EP 2000-941453	20000615 <--
EP 1189904	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000012086	A	20020402	BR 2000-12086	20000615 <--
TR 200103658	T2	20020621	TR 2001-200103658	20000615 <--
JP 2003502331	T2	20030121	JP 2001-503860	20000615
NZ 516031	A	20031031	NZ 2000-516031	20000615
US 6713471	B1	20040330	US 2000-594954	20000615
AT 277048	E	20041015	AT 2000-941453	20000615
ES 2223536	T3	20050301	ES 2000-942807	20000615
ES 2223537	T3	20050301	ES 2000-942808	20000615
ZA 2001009735	A	20040127	ZA 2001-9735	20011127
NO 2001006116	A	20020211	NO 2001-6116	20011214 <--
PRIORITY APPLN. INFO.:			US 1999-139321P P	19990615
			WO 2000-US16498 W	20000615

OTHER SOURCE(S): MARPAT 134:56655
GI



I



II

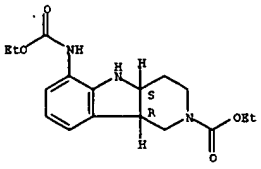
AB Novel γ-carboline compds. of formula I [R1, R2 = H, acyl, alkyl, cycloalkyl, etc.; R3, R4 = H, OH, amino, CF3, alkyl, etc.; R5-R7 = H, halo, CF3, OH, CN, alkyl, aryl, heterocycle, etc.; X = (substituted) NH, (substituted) CONH, (substituted) NHCO, S; A, B, C = (CH2)n, n = 0-3] are prepd. The invention is also concerned with **pharmaceutical** formulations comprising these novel compds. as active ingredients and the use of the novel compds. and their formulations in the treatment of certain disorders. The compds. of this invention are serotonin agonists and antagonists and are useful in the control or prevention of central nervous system disorders including obesity, anxiety, depression, psychosis, schizophrenia, sleep disorders, sexual disorders, migraine, conditions assocd. with cephalic pain, social phobias, and gastrointestinal disorders such as dysfunction of the gastrointestinal tract motility (no data). Thus, II is prepd. starting from p-fluorothiophenol, β-propiolactone and 1-carbethoxy-4-piperidone. **Pharmaceutical** compns. contg. I are described.

L9 ANSWER 10 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

IT 313369-59-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted heterocycle fused γ-carbolines as serotonin agonists and antagonists)

RN 313369-59-4 CA
CN 2H-Pyrido[4,3-b]indole-2-carboxylic acid, 6-[(ethoxycarbonyl)amino]-1,3,4,4a,5,9b-hexahydro-, ethyl ester, (4aR,9bS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

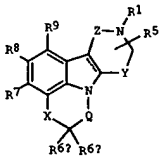


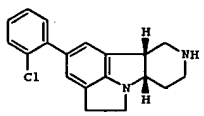
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:56654 CA
TITLE: Preparation of substituted heterocyclo γ-carbolines as serotonin agents
INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei; Mitchell, Ian S.; Chen, Wenting; McClung, Christopher D.; Calvello, Emilie J. B.; Zawrotny, David M.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 388 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077001	A1	20001221	WO 2000-US16375	20000615 <--
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2381322	AA	20001221	CA 2000-2381322	20000615 <--
EP 1189905	A1	20020327	EP 2000-942808	20000615 <--
EP 1189905	B1	20040929		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000012084	A	20020402	BR 2000-12084	20000615 <--
TR 200103658	T2	20020621	TR 2001-200103658	20000615 <--
JP 2003502330	T2	20030121	JP 2001-503859	20000615
US 6713471	B1	20040330	US 2000-594954	20000615
AT 277928	E	20041015	AT 2000-942808	20000615
ES 2223536	T3	20050301	ES 2000-942807	20000615
ES 2223537	T3	20050301	ES 2000-942808	20000615
ZA 2001009735	A	20040127	ZA 2001-9735	20011127
NO 2001006115	A	20020212	NO 2001-6115	20011214 <--
PRIORITY APPLN. INFO.:			US 1999-139321P P	19990615
			WO 2000-US16375 W	20000615

OTHER SOURCE(S): MARPAT 134:56654
GI

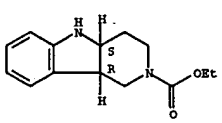

I


II

AB The title compds. I (R1 = acyl, alkyl, alkenyl, alkynyl, cycloalkyl, etc.;

L9 ANSWER 11 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)
R5 = H, alkyl; R6a, R6b = H, OH, amino, CF3, alkyl, alkenyl, alkynyl, alkoxy, haloalkyl, cycloalkyl, aryl; R7 and R9 = H, halo, CF3, OH, cyano, NO2, amino, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, etc.; R8 = H, halo, CF3, CF3O, OH, NO2, cycloalkyl, alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, haloalkyloxy, etc.; X = CO, CH2, alkylmethylene, alkenylmethylene, alkynylmethylene, alkoxymethylene; Q = (CH2)n, n = 0, 1, 2, 3; Y = (CH2)m, m = 0, 1, 2; Z = (CH2)q, q = 1, 2) and their pharmaceutically acceptable salt salts were prepd. Thus, 1-amino-2,3-dihydroindole was treated with 4-piperidone HCl to give 4,5,7,8,9,10-hexahydropyrido[4,3-b]pyrrolo[3,2,1-hi]indole, which was reduced with NaCNBH3, converted to the BOC deriv., brominated, and coupled with 4-chlorophenylboronic acid and deprotected to give the 2-(2-chlorophenyl)octahydropyrido[4,3-b]pyrrolo[3,2,1-hi]indole II. The invention is also concerned with pharmaceutical formulations comprising these novel compds. as active ingredients and the use of the novel compds. and their formulations in the treatment of certain disorders (no data). The compds. of this invention are serotonin agonists and antagonists and are useful in the control or prevention of central nervous system disorders including obesity, anxiety, depression, psychosis, schizophrenia, sleep disorders, sexual disorders, migraine, conditions assocd. with cephalic pain, social phobias, and gastrointestinal disorders such as dysfunction of the gastrointestinal tract motility.
IT 199725-38-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted heterocyclo fused γ-carbolines as serotonin agents)
RN 199725-38-7 CA
CN 2H-Pyrido[4,3-b]indole-2-carboxylic acid, 1,3,4,4a,5,9b-hexahydro-, ethyl ester, (4aR,9bS)-rel- (9CI) (CA INDEX NAME)

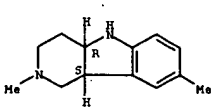
Relative stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

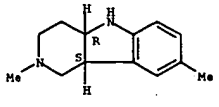
L9 ANSWER 12 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:313480 CA
TITLE: Study of the kinetics of hydrolysis of stobadine acyl derivatives, prodrug forms of scavengers of free oxygen radicals. Part 2: Alkaline hydrolysis
AUTHOR(S): Ondrasova, M.; Stankovicova, Maria; Bezakova, Z.; Benes, L.
CORPORATE SOURCE: Katedra Farm. Chemie, Farm. Fakulta, Univ. Komenskeho, Bratislava, 832 32, Slovakia
SOURCE: Ceska a Slovenska Farmacie (2000), 49(5), 251-255
CODEN: CSLFEK; ISSN: 1210-7816
PUBLISHER: Ceska Lekarska Spolecnost J. Ev. Purkyne
DOCUMENT TYPE: Journal
LANGUAGE: Slovak
AB Stobadine is a a potential antiarrhythmic, antihistaminic, anesthetic, and antiulcer pharmacol agent with marked antioxidant effects. Stobadine N5 acyl substitution yielded derivs., which represent prodrug forms of the active agent stobadine. They acyl derivs. may be hydrolyzed in the body and the active agent may be released in higher concns. in various target biol. tissues. The hydrolysis kinetics of 12 stobadine acyl derivs. was studied in 0.1 M NaOH at 70°C, using UV spectrophotometry. The hydrolysis rate consts. were correlated with the length of the acyl side-chain and the pKa values of the particular compds.
IT 85202-17-1D, Stobadine, acyl derivs.
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(stobadine acyl derivs. alkaline hydrolysis as model of release of free oxygen radical scavengers from prodrugs and its kinetics)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L9 ANSWER 13 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:98957 CA
TITLE: Extraction and chromatographic separation methods in pharmacokinetic studies of stobadine - an indole-related antioxidant and free-radical scavenger
AUTHOR(S): Soltes, L.; Bezek, S.; Ujhazy, E.; Bauer, V.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-84216, Slovakia
SOURCE: Biomedical Chromatography (2000), 14(3), 188-201
CODEN: BICHE2; ISSN: 0269-3879
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with over 80 refs. This overview provides comprehensive information on the most relevant results of Stobadine preclin. disposition studies. In order to investigate pharmacokinetic processes of the drug in rats, dogs and in human volunteers, several bioanal. assays based on radiometric, spectrofluorometric, as well as chromatog. determination methods were developed and implemented. In small laboratory animals, the drug absorption, distribution, metabolism and elimination were investigated by administering 3H-labeled Stobadine. Spectrofluorometry was used alternatively for the determination of cold/unlabeled Stobadine in exts. of biomaterials sampled from larger animal species. The chromatog. separation methods proved, however, to be the most advantageous for determining details of the drug disposition and fate in the body.
IT 95751-51-2, Stobadine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(extraction and chromatog. separation methods in pharmacokinetic studies of stobadine)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



●2 HCl

REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:790 CA
TITLE: New use of glutamate antagonists for the treatment of cancer
INVENTOR(S): Ikonomidou, Hrissanthi
PATENT ASSIGNEE(S): Germany
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

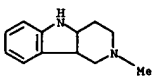
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1002535	A1	20000524	EP 1998-250380	19981028 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9964750	A1	20000515	AU 1999-64750	19991022 <--
EP 1124553	A1	20010822	EP 1999-952622	19991022 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002528415	T2	20020903	JP 2000-578005	19991022 <--
US 6797692	B1	20040928	US 2001-830354	20010425
US 2005054619	A1	20050310	US 2004-912159	20040806
US 2005054650	A1	20050310	US 2004-912175	20040806

PRIORITY APPLN. INFO.: EP 1998-250380 A 19981028
WO 1999-EP8004 W 19991022
US 2001-830354 A3 20010425

AB New therapies can be devised based upon a demonstration of the role of glutamate in the pathogenesis of cancer. Inhibitors of the interaction of glutamate with the AMPA, kainate, or NMDA receptor complexes are likely to be useful in treating cancer and can be formulated as pharmaceutical compns. They can be identified by appropriate screens.

IT 56223-47-3D, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glutamate antagonists for cancer treatment)

RN 56223-47-3 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:273805 CA
TITLE: Overview of stobadine bioanalysis: evaluation and application in pharmacokinetics
AUTHOR(S): Bauerova, K.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia
SOURCE: European Journal of Drug Metabolism and Pharmacokinetics (1999), 24(3), 237-242
CODEN: EJDPD2; ISSN: 0378-7966
PUBLISHER: Medecine et Hygiene
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Besides its many pharmacodynamic actions, the pyridoindole stobadine was found to exert antioxidant activity and thus possesses the potential to protect various tissues against oxidative stress. This overview is focussed on both the evaluation of the chemical procedures used in the bioassay of stobadine and its metabolites and on the comparison of their quality in the light of applicability for preclin. and clin. pharmacokinetic expts. All methods and applications were performed at the Institute of Exptl. Pharmacol., SASc in Bratislava, Slovakia. In pharmacokinetic and toxicokinetic studies, [3H]-labeled stobadine dihydrochloride was administered i.v. or orally to rats in single and repeated doses. Liquid-liquid extraction was used for selective isolation of stobadine and its metabolites from biol. matrix, followed by liquid scintillation quantification. A TLRC method was developed both to check the radiochem. purity of [3H]-stobadine and to quantify the labeled drug in rat plasma. A spectrofluorometric approach was used for determination of stobadine in dog serum and urine after its administration in the form of either the dihydrochloride or the dipalmitate. The method allowed us to perform a bioavailability study and a long-term toxicol. study. The HPLC method with a limit of detection of 10 ng/mL of plasma proved suitable for calculating the compartmental pharmacokinetic parameters of both salt forms of stobadine administered to dog and man. This method was based on solid-phase extraction procedure by using Separcol SI C18 cartridges. In a GC method, the combination of capillary column separation and nitrogen-specific detection permitted the assay of serum stobadine concns. as low as 5 ng/mL. The detection limit of the GC/MS method was 1 ng/mL of plasma or of phosphate buffer saline. This method was used for a bioequivalence study of two stobadine dipalmitate dosage forms and for a transdermal penetration study of stobadine acyl derivs. All the developed assays proved to be appropriate for low-concentration determination of stobadine in a wide range of pharmacokinetic studies.

IT 85202-18-2, Stobadine dipalmitate
RL: ANT (Analyte); ANST (Analytical study)
(stobadine bioanal.: comparative evaluation ov various anal. procedures for pharmacokinetic study)

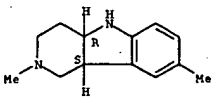
RN 85202-18-2 CA
CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)

CM 1

L9 ANSWER 15 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

CRN 85202-17-1
CMF C13 H18 N2

Absolute stereochemistry. Rotation (-).



CM 2

CRN 57-10-3
CMF C16 H32 O2

$HO_2C-(CH_2)_{14}-Me$

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:202577 CA
TITLE: Bioavailability and pharmacokinetic studies in the development of an oral formulation of stobadine dipalmitate
AUTHOR(S): Bauerova, K.; Bohov, P.; Durisova, M.; Bezek, S.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (1999), 21(7), 499-503
CODEN: MFEPDX; ISSN: 0379-0355
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pyridoindole stobadine is a novel drug with antioxidant and cardioprotective properties. The objective of this study was to compare the bioavailability and the main pharmacokinetic parameters of two different stobadine dosage forms, STBtest and STBref, after single oral dosing in the form of gelatine capsules to 6 dogs. The dose ranged from 2.9 to 4.7 mg/kg and a randomized two-period crossover design was applied. To quantify the drug in plasma, a GC/MS method was developed with a quantification limit of 1 ng/mL. The time profiles of stobadine plasma concns. were fitted by pharmacokinetic models. The extent of relative bioavailability ranged between 0.71 and 1.56. Practically no difference was found between the bioavailability rate of the two capsules, expressed as Cmax/AUC, with values ranging from 0.0022-0.0047 min-1 for STBtest and 0.0022-0.0045 min-1 for STBref. In conclusion, the technol. difference of the capsules investigated did not yield deviations in either their extent or rate of absorption. Therefore the two stobadine formulations were concluded to be bioequivalent.

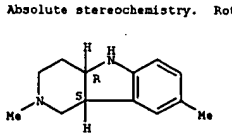
IT 85202-18-2, Stobadine dipalmitate
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(bioavailability and pharmacokinetic studies in development of oral formulation of stobadine dipalmitate)

RN 85202-18-2 CA
CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 85202-17-1
CMF C13 H18 N2

Absolute stereochemistry. Rotation (-).



CM 2

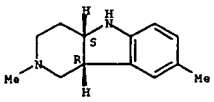
CRN 57-10-3
CMF C16 H32 O2

L9 ANSWER 16 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

$HD_2C-(CH_2)_{14}-Me$

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



●2 HCl

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 134 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 132:132216 CA
TITLE: Dopaminergic involvement in the process of reinforcement from diethyl ether vapor in rats
AUTHOR(S): Pogorelov, Vladimir M.; Kovalev, Georgy I.
CORPORATE SOURCE: Laboratory of Radioisotopic Researches, Institute of Pharmacology, Russian Academy of Medical Sciences, Moscow, Russia
SOURCE: Progress in Neuro-Psychopharmacology & Biological Psychiatry (1999), 23(6), 1135-1156
CODEN: PNPPD7; ISSN: 0278-5846
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1. Male and female Wistar rats were placed in boxes for 30 min daily and allowed to nose-poke in two holes on opposite walls, which opened into evaporation chambers through valves. One chamber contained di-Et ether vapor another - air, the contents being alternated randomly. Rats inhaled the contents of evaporation chambers while nose-poking differed by the level of intake of di-Et ether vapor. Rats with the intake time of more than 3 s formed about 15% of population. Their preference for di-Et ether was above 0.55. There was significant neg. correlation between the time of vapor inhalation and the time of immobility in forced swimming test in females but not in males. Withdrawal of di-Et ether vapor decreased the inhalation time. On the first day after ether deprivation inhalation time rose above average level. Relationship between concentration of ether vapor and the time of its inhalation was inverted U-shaped function. Substitution of acetone vapor elevated the time of the vapor inhalation. D-amphetamine in dose 0.05 mg/kg elevated the time of inhalation of and preference for ether vapor in some rats. In doses 0.05-1.0 mg/kg amphetamine selectively suppressed the time of vapor inhalation. Haloperidol in doses 0.05 and 0.1 mg/kg elevated the time of vapor inhalation on the first day in females and suppressed it in doses 0.05-0.3 mg/kg dose-dependently on the second day. Atypical neuroleptic cis-carbidine elevated the time of vapor inhalation in doses 2.5 and 5.0 mg/kg and suppressed it at 10 mg/kg. Di-Et ether vapor can be established as reinforcer in rats. Female rats are more liable to reinforcement from ether vapor than males and show more pronounced response to haloperidol. This may be related to its more active behavior in the forced swimming situation. The results point to potential involvement of dopamine system in the process of reinforcement from ether vapor.

IT 94452-31-0, cis-Carbidine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dopaminergic involvement in reinforcement from di-Et ether vapor)

RN 94452-31-0 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L9 ANSWER 18 OF 134 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 132:117462 CA
TITLE: Effects of stobadine, melatonin, and other antioxidants on hypoxia/reoxygenation-induced synaptic transmission failure in rat hippocampal slices
AUTHOR(S): Vlkolinsky, Roman; Stolc, Svorad
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-842 16, Slovakia
SOURCE: Brain Research (1999), 850(1,2), 118-126
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

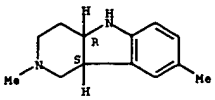
AB In vitro reversible ischemia was simulated with rat hippocampal slices in order to test the neuroprotective activity of selected antioxidants with emphasis on the pyridoindole stobadine. Slices were exposed to hypoxia (HYP) combined with lowered D-glucose concentration to induce synaptic transmission (ST) failure, which turned out to be irreversible in approx. 80%-100% of slices during reoxygenation (ROX). The amplitude of population spikes (PoS) evoked transsynaptically by elec. stimulation of Schaffer collaterals and recorded in CA1 neurons was the parameter of ST. Pretreatment of slices with stobadine dissolved in slice superfusion media (1 to 100 μM) improved ST recovery after 20-min tissue ROX. Stobadine decreased the number of irreversibly damaged slices and increased the average amplitude of PoS during tissue ROX. The concentration-response relationship of protective activity was bell-shaped, with maximum at 3-30 μM. Moreover, the half-time of PoS decay (t1/2) during HYP was significantly delayed in stobadine treated groups (10 to 100 μM). The neurohormone melatonin (30 to 100 μM) and 21-aminosteroid U-74389G (10 μM) revealed similar protective activity on ST recovery and on t1/2 during HYP. Trolox (200 μM) improved the PoS recovery, yet it had no effect on t1/2. The iron chelator deferoxamine (250 and 500 μM) had no protective effects at all. α-Tocopherol administered to animals orally (200 mg/kg for 10 days) only marginally improved the PoS recovery. Comparing the protective effect of compds. tested on PoS recovery, we assume the following rank order of potency: U-74389G > stobadine > melatonin >> trolox. Our findings suggest that stobadine as well as trolox, U-74389G and melatonin, antioxidants with remarkably different chemical structures, exerted neuroprotective activity, probably determined by antioxidative properties of these compds. Moreover, stobadine, U-74389G, and melatonin were able to delay the early ST decay during HYP, which might indicate improved energetic state of neurons in the treated tissue. The study supports the notion about the neuroprotective activity of certain antioxidants.

IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of stobadine, melatonin, and other antioxidants on hypoxia/reoxygenation-induced synaptic transmission failure in rat hippocampal slices)

RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L9 ANSWER 18 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 134 CA COPYRIGHT 2005 ACS on STN

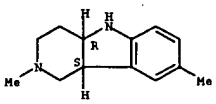
ACCESSION NUMBER: 132:73608 CA
TITLE: Evaluation of long-term administration of the antioxidant stobadine on exploratory behavior in rats of both genders
AUTHOR(S): Dubovicky, M.; Ujhazy, E.; Kovacovsky, P.; Rychlik, I.; Jansak, J.
CORPORATE SOURCE: Institute of Experimental Pharmacology SASc, Bratislava, 842 16, Slovakia
SOURCE: Journal of Applied Toxicology (1999), 19(6), 431-436
CODEN: JJATDK; ISSN: 0260-437X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Stobadine (STO) is a prospective neuro- and cardioprotective drug with high antioxidative properties. The aim of this study was to ascertain the effect of long-term administration of STO on exploratory behavior and habituation processes in adult virgin female and male rats. Stobadine was administered by oral gavage in a single dose of 50 mg kg-1 day-1 for a total of 56 days. The animals were tested for exploratory behavior-intensity of motor and vertical activity in an open field test in three blocks of measurements (initial screening; after 56 days of STO administration; and 28 days after the last treatment). The rate of decline of motor activity was evaluated during four consecutive days of testing (interrupted habituation). Administration of STO resulted in transient inhibition of exploratory behavior in female rats without overtly detectable toxicity. Exploratory behavior of males was not affected by STO treatment.

IT 95751-51-2, Stobadine
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of long-term administration of the antioxidant stobadine on exploratory behavior in rats of both genders)

RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



●2 HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 134 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 132:18356 CA
TITLE: Pharmacokinetic study of stobadine
AUTHOR(S): Bezek, S.; Soltes, L.; Scasnar, V.; Bauerova, K.; Kallay, Z.; Durisova, M.; Mihalova, D.; Bohov, P.; Faberova, V.; Kukan, M.; Trnovec, T.; Koprda, V.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 2003-2005
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 16 refs. The most important results of stobadine pharmacokinetic studies in rats, dogs, and humans are presented. Stobadine dihydrochloride and stobadine dipalmitate were used for i.v. and oral administration, resp. TLC, HPLC, GLC, GC-MS, radiometric, and fluorometric methods were developed for the studies of stobadine and its metabolites.

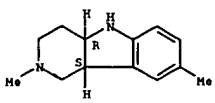
IT 85202-18-2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(stobadine pharmacokinetics in rats, dogs and humans)

RN 85202-18-2 CA
CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 85202-17-1
CMF C13 H18 N2

Absolute stereochemistry. Rotation (-).



CM 2

CRN 57-10-3
CMF C16 H32 O2

$HO_2C-(CH_2)_{14}-Me$

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 134 CA COPYRIGHT 2005 ACS on STN

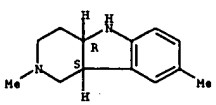
ACCESSION NUMBER: 132:8961 CA
TITLE: Membrane ion transport systems during oxidative stress in rodent brain: protective effect of stobadine and other antioxidants
AUTHOR(S): Lehotsky, J.; Kaplan, P.; Racay, P.; Matejovicova, M.; Drgova, A.; Mezesova, V.
CORPORATE SOURCE: Jessenius Medical Faculty, Comenius University, Martin, SK-03601, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 1951-1958
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of oxidative stress in vitro induced by radical generating systems (RGS) (Fe2+-EDTA and Fe2+-EDTA plus H2O2) on synaptosomal and microsomal ion transport systems as well as on the membrane fluidity was investigated. Oxidative insult reduced Na+,K+-ATPase activity by 50.7% and Na+-dependent Ca2+ uptake measured in choline media by 46.7%. Membrane fluidity was also significantly reduced as observed with the fluorescent probe. Stobadine (ST) prevented the decrease in membrane fluidity and Na+-dependent Ca2+ uptake, however Na+,K+-ATPase activity was only partially protected, indicating a more complex mechanism of inhibition. Incubation of microsomes with RGS led to the loss of ability of membranes to sequester Ca2+, as well as to the decrease of Ca2+-ATPase activity and to the increase of Ca2+ permeability to 125.1%. The relative potency of the two RGS to decrease membrane fluidity correlated well with the system's potencies to induce lipid peroxidn. The extent of protection against depression of Ca2+ uptake values and Ca2+-ATPase activity by membrane soluble antioxidants (U-74500A, U-83836E, t-butylated hydroxytoluene-BHT and ST) was dependent on the exptl. conditions and on the dose and nature of antioxidant used. ST seems to be at least as affective as BHT and 21-aminosteroids, and more potent than tocopherol acetate. Water soluble glutathione had no significant effect on the RGS induced inhibition of Ca2+-ATPase activity. Combination of ST with glutathione enhanced ST antioxidant efficacy, so drug combination might be beneficial therapeutically.

IT 95751-51-2, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective effect of stobadine and other antioxidants on membrane ion transport systems during oxidative stress in rodent brain)

RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



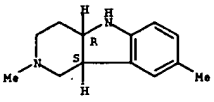
●2 HCl

L9 ANSWER 21 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 22 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:8959 CA
TITLE: EPR spectroscopy of free radical intermediates of antiarrhythmic-antihypoxic drug stobadine, a pyridoindole derivative
AUTHOR(S): Misik, Vladimir; Ondrias, Karol; Stasko, Andrej
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 1879-1881
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mechanisms of antioxidant action of stobadine, a pyridoindole derivative with cardioprotective and antihypoxic properties, has been probed using EPR spectroscopy. Oxidation of stobadine by PbO2/tBuOOH in benzene results in the formation of nitroxide radical observable directly by EPR spectroscopy at room temperature, indicating conversion of indolic amino group to the corresponding nitroxide.
IT 95751-51-2, Stobadine
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(EPR of free radical intermediates of antiarrhythmic-antihypoxic drug stobadine)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

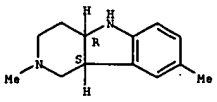


●2 HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:8957 CA
TITLE: Stobadine: bellwether of a broader view of drug actions
AUTHOR(S): Vincenzi, Frank F.; Hinds, Thomas R.
CORPORATE SOURCE: Department of Pharmacology, University of Washington, Seattle, WA, 98195-7280, USA
SOURCE: Life Sciences (1999), 65(18/19), 1857-1864
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Stobadine was recognized early in its development as having antioxidant properties. A number of labs. found assocns. between the antioxidant properties of stobadine and its potential beneficial effects. We found that stobadine acted as an antioxidant in a modification of an oxygen radical absorbance capacity assay. Similar results were observed with other drugs, including tirilazad and pramipexole. We suggest that stobadine and certain other drugs exhibit antioxidant properties in both hydrophilic and hydrophobic environments. Other drugs have been developed for their antioxidant properties and some currently marketed drugs have antioxidant properties. Although they may not have been explicitly sought during development, at least some of the beneficial effects may be related to antioxidant properties and/or scavenging of free radicals. Because stobadine was one of the first drugs for which useful properties were associated with its antioxidant actions, stobadine may be seen as a bellwether of a broader view of pharmacol. actions - a view that encompasses antioxidant properties as a useful basis of therapeutic effects.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stobadine: bellwether of a broader view of antioxidant drug actions)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

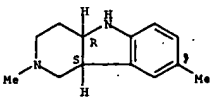
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:8879 CA
TITLE: Oxidative modification of serum albumin in an experimental glycation model of diabetes mellitus in vitro: effect of the pyridoindole antioxidant stobadine
AUTHOR(S): Stefek, M.; Krizanova, L.; Trnkova, Z.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 1995-1997
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Under conditions of an exptl. in vitro glycation model, the pyridoindole antioxidant stobadine significantly inhibited glycation-related fluorescence changes of bovine serum albumin as well as the yield of 2,4-dinitrophenyl-hydrazine-reactive carbonyls with an efficacy comparable to that of the reference antioxidants Trolox C and 2-keto-4-methiolbutyric acid, and more efficiently than did aminoguanidine. Since stobadine did not affect the covalent binding of glucose, the protective effect may be explained by the ability of the drug to eliminate free radical intermediates of glyco-oxidation reactions, operative after the preceding glycation steps.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyridoindole antioxidant stobadine effect on oxidative modification of serum albumin in glycation model of diabetes mellitus)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



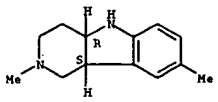
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:8624 CA
TITLE: Indole derivatives as neuroprotectants
AUTHOR(S): Stolc, Svorad
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-842 16, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 1943-1950
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 69 refs. It seems to be satisfactorily proved that reactive oxygen species (ROS) participate in numerous pathol. processes in the nervous system (NS). Compds. able to interfere with the action of ROS might be useful in prevention and treatment of these pathologies. The search is focused on compds. with a suitable spectrum of pharmacol . and pharmacokinetic properties, among which indole derivs. are distinct group with great potential to be further developed. The paper presents an overview of indole derived compds. in which protective action has been demonstrated in the NS in situations in which ROS are excessively generated, such as chemical induced oxidative stress, hypoxia/reoxygenation, ischemia/reperfusion. These compds. include indoleamines (melatonin), carbazoles (carvedilol), carbolines (tetrahydrocarbolines, pyrimidoindoles, vinpocetine). Special attention is paid to the γ-carboline stobadine. A range of effects which seem to be associated with its neuroprotective actions (antioxidant and ROS scavenging effects, capability to pass the hematoencephalic barrier, pharmacokinetic properties, etc.) are considered. A novel compound with pyrimidoindole structure (U-101033E) is mentioned. Attention is drawn also to the neurotoxic potential demonstrated in some carbolines (2-amino-α-carboline, halogenated tetrahydro-β-carboline "TaClo", harmane, norharmane). The indole nucleus seems to be a promising basis for design and synthesis of new derivs. able to protect the NS against oxidative stress in a variety of acute and chronic NS pathologies.

IT 95751-51-2, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(indole derivs. as neuroprotectants)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



●2 HCl

L9 ANSWER 25 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

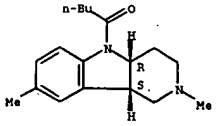
REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 26 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:3153 CA
TITLE: Kinetics of hydrolysis of acetyl, valeroyl and nicotinoyl acyl derivatives of stobadine
AUTHOR(S): Stankovicova, M.; Bezakova, Z.; Benes, L.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Faculty of Pharmacy of Comenius University, Bratislava, 832 32, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 2007-2010
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present work deals with the kinetics of hydrolysis of the acyl derivs. of stobadine, an originally synthesized potential antiarrhythmic and antihypoxic drug, which was found to have also an excellent scavenging effect on reactive oxygen species. The acyl derivs. of stobadine, which possess high lipophilicity, represent model blood-brain barrier penetrating agents. It is assumed that the acyl derivs. of stobadine may act as prodrugs which are hydrolyzed in different biol. tissues to release the active drug. The decomposition of three acyl derivs. of stobadine was studied in acidic, basic and neutral buffer solns. at constant ionic strength (0.1 mol/L) at 25° and 70°C using UV spectrophotometric method. The pseudo first-order rate consts. and the pH-rate profile for the degradation of acetyl, valeroyl, and nicotinoyl derivs. of stobadine were determined Confirmation that stobadine was the first degradation product was provided by thin-layer chromatog.

IT 201608-29-9
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(kinetics and mechanism of hydrolysis of acetyl, valeroyl. and nicotinoyl acyl derivs. of stobadine)
RN 201608-29-9 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-5-(1-oxopentyl)-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



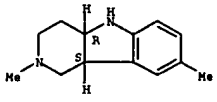
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 27 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:349826 CA
TITLE: Reactive oxygen species induced smooth muscle responses in the intestine, vessels and airways and the effect of antioxidants
AUTHOR(S): Bauer, V.; Sotnikova, R.; Machova, J.; Matyas, S.; Pucovsky, V.; Stefek, M.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 1909-1917
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Numerous exptl. data confirm the importance of reactive oxygen species (ROS) in physiol. activities of smooth muscles and in the pathogenesis of various diseases with altered function of smooth muscles. The present study shows that smooth muscles of the intestine, airways and vessels, as well as their epithelium, endothelium and innervations, might be important targets of the ROS action. We demonstrated differences among the actions of various ROS (endogenous, exogenous, produced enzymically, non-enzymically) as well as among their actions in different smooth muscle tissues. Our results indicate that ROS are involved in changes in muscle tone, membrane conductance, calcium homeostasis, calcium-dependent processes, as well as in eicosanoid and nitric oxide metabolism The effects of antioxidative enzymes (superoxide dismutase, catalase), of several drugs of natural origin (e.g. Kampo Medicines) and synthetic agents (e.g. stobadine, nitroxopine, ACE inhibitors) suggest that smooth muscle tissues are useful models to study ROS action and drug intervention in ROS induced injuries.

IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(intestine, blood vessels and airway smooth muscle responses to reactive oxygen species and effect of antioxidants)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

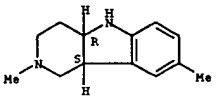
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 28 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:346326 CA
TITLE: Protective effect of stobadine in experimental colitis
AUTHOR(S): Nosalova, Viera; Bauer, Viktor
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 1919-1921
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To assess the role of reactive oxygen species in inflammatory bowel disease, the effects of the antioxidant and free radical scavenger drug stobadine were studied in acetic acid-induced exptl. colitis in male Wistar rats. Stobadine given locally into the colon decreased the colonic mucosal injury, abolished the increase in myeloperoxidase activity, attenuated the enhanced vascular permeability, and prevented the depletion of reduced glutathione. The decrease in free radical production and oxidative damage in the inflamed colonic mucosa may be used as a complementary treatment in ulcerative colitis.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stobadine protective effects in exptl. colitis in rats)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

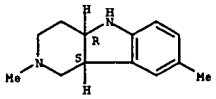
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 29 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:346287 CA
TITLE: Placental transfer of stobadine in rabbits
AUTHOR(S): Ujhazy, E.; Dubovicky, M.; Soltes, L.; Faberova, V.; Zemanek, M.; Gajdosik, A.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 2011-2014
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Stobadine, a pyridoindole antioxidant, was investigated for its placental transfer and distribution in New Zealand white rabbits on the 27th day of gestation. The concns. of stobadine were determined in maternal and fetal organs (plasma, brain, heart) at 30, 60, 120, and 360 min after oral administration of the drug in a dose of 5 mg/kg. The results obtained proved that after oral stobadine intake by rabbits at the stage of advanced pregnancy both maternal and fetal organs were under a certain drug level which could act protectively against oxidative stress - frequently occurring during late organogenesis, fetal stages and delivery, as well as during early postnatal development.
IT 85202-17-1, Stobadine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(placental transfer of stobadine)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

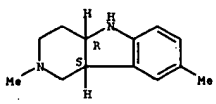
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 30 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:346285 CA
TITLE: Aggregation of human blood platelets in the presence of the pyridoindole stobadine
AUTHOR(S): Jancinova, Viera; Nosal, Rado; Danihelova, Edita
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 1983-1986
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of stobadine dihydrochloride, an antiarrhythmic and cardioprotective drug with antioxidant and neuroprotective properties, were studied in assays of human blood platelet in vitro aggregation. Pretreatment of platelets with stobadine for 30 s inhibited the stimulated platelet aggregation in a dose-dependent way. Depending on the aggregation stimulus used, the minimal effective concns. of the drug were 1 μM (adrenaline), 200 μM (ADP), and 1000 μM (PMA). Aggregation induced with thrombin or the Ca2+-ionophore A-23187 was not changed in the presence of stobadine even at 1000 μM. Addition of stobadine 30 s after adrenaline was also effective and terminated the aggregation (100 and 1000 μM) or delayed the onset of its second phase (10 μM). Thus, stobadine is a potent inhibitor of adrenaline-induced blood platelet aggregation, indicating an involvement in the antithrombotic and cytoprotective activities.
IT 95751-51-2, Stobadine dihydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(stobadine inhibition of human blood platelet aggregation in vitro)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

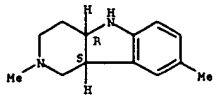


●2 HCl

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:346280 CA
TITLE: Effect of stobadine on cardiac injury induced by ischemia and reperfusion
AUTHOR(S): Knezl, V.; Sotnikova, R.; Okruhlicova, L.; Navarova, J.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 1931-1933
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of the antioxidant drug stobadine on ischemia/reperfusion injury were studied in the isolated Langendorff rat heart prepns. Ischemia was induced by 30-min stop-flow and the reperfusion lasted 30 min. Reperfusion of the ischemic heart induced dysrhythmias, with the most severe ones occurring in the first minutes of reperfusion. An increase in coronary perfusion pressure was observed after 15 min of reperfusion. Stobadine (10-6 M applied 3 min before the onset of ischemia and during reperfusion) prevented the deleterious effects to develop fully. The protective effects of stobadine seem to be due to its antioxidant properties.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(stobadine protective effects in ischemia and reperfusion injury in isolated rat hearts)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

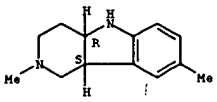
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 32 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:346279 CA
TITLE: Stobadine inhibits lysosomal enzyme release in vivo and in vitro
AUTHOR(S): Navarova, Jana; Macickova, Tatiana; Horakova, Katarina; Urbancikova, Miroslava
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 1905-1907
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of stobadine dihydrochloride, a cardioprotective drug with antiarrhythmic, antihypoxic and oxygen free radical scavenging properties, to protect cells against cyclophosphamide-induced toxic and cytotoxic damage was studied in vivo and in vitro. The cyclophosphamide toxic damage in female ICR mice was accompanied by marked increase in the activity of lysosomal enzymes (acid phosphatase, N-acetyl-β-D-glucosaminidase) in the spleen and kidney. Administration of stobadine prior to cyclophosphamide inhibited these biochem. changes. The in vivo protective effects of stobadine were comparable with the in vitro effects in HeLa cells.
IT 95751-51-2, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(stobadine inhibits lysosomal enzyme release from mouse spleen and kidney and from HeLa cells in vitro)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

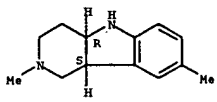


●2 HCl

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 33 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:345989 CA
TITLE: Antimutagenic effects of stobadine: review of results
AUTHOR(S): Chorvatovicova, Darina; Horvathova, Eva; Slamenova, Darina
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia
SOURCE: Life Sciences (1999), 65(18/19), 2015-2017
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 14 refs. which summarizes the results of previously published studies testifying the hypothesis of the antimutagenic effect of stobadine (STB) in vivo and in vitro. The micronucleus test was used in in vivo expts. with ICR mice. Oral pretreatment with STB significantly decreased the mutagenic effect of cyclophosphamide (CP) in a concentration-dependent way. The protective effect of
STB was confirmed in fetuses of CP-treated mice. STB pretreatment exerted also a radioprotective effect in Co60-irradiated mice. The ineffectiveness of STB posttreatment is indicative of its effect operative in the initiation of mutagenesis and of its radical-scavenging mechanism. The ability of STB to reduce N-methyl-N'-nitro-N-nitrosoguanidine (MNNG)-induced gene mutations and MNNG-induced calcinosis/Raynaud's phenomenon/esophageal dysmotility/sclerodactyly/telangiectasia variant of scleroderma(CREST)-pos. and CREST-neg. micronuclei in V-79 cells was tested in in vitro expts. It was found that this drug reduced the level of both gene mutations and CREST-neg. micronuclei mainly if given as pretreatment before exposure of cells to MNNG. Thus, STB may have inhibited mutagenesis not only by scavenging reactive oxygen species, but also as a result of the induction of metabolic enzymes, which reduced the level of DNA lesions.
IT 85202-17-1, Stobadine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimutagenic effects of stobadine)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

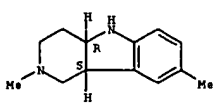
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 34 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 130:162954 CA
TITLE: Endothelial protective effect of stobadine on ischemia/reperfusion-induced injury
AUTHOR(S): Sotnikova, R.; Okruhlicova, L.; Noskovic, P.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia
SOURCE: General Physiology and Biophysics (1998), 17(3), 253-264
CODEN: GPBIEZ; ISSN: 0231-5882
PUBLISHER: Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of the present study was to evaluate the influence of the antioxidant stobadine on changes in the reactivity of the rat abdominal aorta induced by ischemia and reperfusion (I/R). In anesthetized male rats, in vivo ischemia was elicited by occlusion of the abdominal aorta for 18 h; reperfusion lasted 30 min. The aortal rings were taken from the reperfused portion. Decreased relaxant response to acetylcholine, as a consequence of endothelial injury, was seen after I/R. We also demonstrated I/R-induced reversible ultrastructural changes both in endothelial and smooth muscle cells, predominantly in the mitochondria. Lipid peroxidn. was increased in homogenates of I/R aortae; the concentration of
thiobarbituric acid reactive substances (TBARS) increased from a control value of 0.97 ± 0.03 to 2.57 ± 0.06 nmol/l/mg protein. Stobadine (2 mg/kg i.v., 5 min before starting reperfusion) protected the abdominal aorta against I/R-induced decrease of acetylcholine relaxation, and prevented changes in mitochondria and an increase of TBARS concentration The
protective effect of stobadine seems to be due to its antioxidant properties.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(endothelial protective effect of stobadine on ischemia/reperfusion-induced injury)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

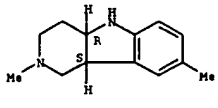
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 35 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 130:60575 CA
TITLE: Studies of the kinetics of hydrolysis of acyl derivatives of stobadine, the prodrug forms of oxygen free radical scavengers. Part 1: acid hydrolysis
AUTHOR(S): Stankovicova, M.; Bezakova, Z.; Benes, L.
CORPORATE SOURCE: Katedra farmaceutickej chemie Farmaceutickej fakulty, Univerzity Komenskeho, Bratislava, Slovakia
SOURCE: Ceska a Slovenska Farmacie (1998), 47(5), 239-242
CODEN: CSLFEK; ISSN: 1210-7816
PUBLISHER: Ceska Lekarska Spolecnost J. Ev. Purkyne
DOCUMENT TYPE: Journal
LANGUAGE: Slovak
AB Stobadine, (-)-cis-2,8-dimethyl-2,3,4,4a,5,9a-hexahydro-1H-pyrido[4,3b]-indole, is a substance with potential antiarrhythmic and antihypoxic effects, in which also a marked radical-scavenging effect has been found. Stobadine acyl derivs. were prepared and it is assumed that the active principle will be released from them by hydrolyzing in various biol. tissues. The present paper examines the kinetics of acid hydrolysis of 13 stobadine derivs. Decomposition of substances was studied in the medium of hydrochloric acid 0.1 mL.l-1 at 20 and 70 °C spectrophotometrically in the UV region and rate consts. of hydrolysis were determined The methods of
thin-layer and gas chromatog. confirmed that stobadine is released from the prodrug form.
IT 85202-17-1D, Stobadine, acyl derivs.
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(kinetics of hydrolysis of acyl derivs. of stobadine, the prodrug forms of oxygen free radical scavengers)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L9 ANSWER 36 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 129:23 CA
TITLE: Antioxidant and pharmacodynamic effects of pyridoindole stobadine
AUTHOR(S): Horakova, L'.; Stolc, S.
CORPORATE SOURCE: Institute Experimental Pharmacology, Slovak Academy Sciences, Bratislava, SK-842 16, Slovakia
SOURCE: General Pharmacology (1998), 30(5), 627-638
CODEN: GEPHHP; ISSN: 0306-3623
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with many refs. 1. The review summarizes the most important data known so far on chemical, pharmacodynamics, toxicol. and clinics of the investigational agent, pyridoindole stobadine. 2. Stobadine was shown to be able to scavenge hydroxyl, peroxyl and alkoxyl radicals, to quench singlet oxygen, to repair oxidized amino acids and to preserve oxidation of SH groups by one-electron donation. These effects originated from its ability to form a stable nitrogen-centered radical on indole nitrogen. Consequently, it was able to diminish lipid peroxidn. and protein impairment under oxidative stress. 3. In various in vitro and in vivo animal models, stobadine was shown to diminish the impairment of the myocardium induced by mechanisms involving reactive oxygen species (e.g., myocardial infarction, hypoxia/reoxygenation, catecholamine overexposure). 4. The neuroprotective effect of stobadine was demonstrated in a series of in vivo and in vitro models (brain in situ, brain slices, spinal cord, autonomic ganglia, etc.) during ischemia/reperfusion and hypoxia/reoxygenation or in the presence of chemical systems generating free oxygen radicals, and so forth. Stobadine improved animal survival rate and synaptic transmission recovery, maintained SH tissue level and diminished lipid peroxidn. as well as impairment of Ca-sequestering intracellular systems. 5. Oxidation of low-d. lipoproteins (LDLs), which plays a major role in the development of atherosclerosis, was decreased by stobadine in vitro. Both lipid and protein (apo B) components of LDL were protected against Cu2+-induced oxidation by this agent. 6. Stobadine proved to be an effective protectant in models of free radical pathol. in vivo, such as cyclophosphamide-, MNNG- or 60Co-induced mutagenesis and alloxan-induced hyperglycemia. 7. Besides other remarkable pharmacodynamic effects, stobadine exerts antidysrhythmic, local anesthetic, α-adrenolytic, antihistaminic, myorelaxant and antiulcerogenic actions. 8. Pharmacokinetic analyses demonstrated that stobadine was readily absorbed from the gastrointestinal tract. Thanks to its balanced lipo-hydrophilic properties, it was distributed over both water and lipid phases in biol. tissues. It was shown to easily penetrate the blood-brain barrier. 9. Acute, subchronic and chronic toxicity studies in several animal species, as well as numerous analyses of embryotoxicity, teratogenicity, mutagenicity and genotoxicity, revealed only a negligible toxic potential of this agent. 10. Phase-one clin. study demonstrated safety of the compound Only slight side effects-namely, a slight hypotension and a slight sedative effect-were observed subsequent to the highest dose used. In phase-two clin. study, the patients with angina pectoris treated for 4 wk with stobadine showed a significant decrease in the frequency of anginal attacks, in the number of self-administrations of sublingual nitroglycerin and in plasma lipoprotein, cholesterol and triglyceride levels. A slight decrease in systolic and diastolic blood pressure also was observed 11. It is suggested

L9 ANSWER 36 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)
that stobadine may be considered a contribution to the search for new effective cardio- and neuroprotectants based on antioxidant or free radical scavenging mechanisms of action.

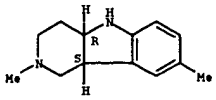
IT 85202-18-2, DP 1031
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antioxidant and pharmacodynamic effects of pyridoindole stobadine)

RN 85202-18-2 CA
CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 85202-17-1
CMF C13 H18 N2

Absolute stereochemistry. Rotation (-).



CM 2

CRN 57-10-3
CMF C16 H32 O2

REFERENCE COUNT: 139 THERE ARE 139 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

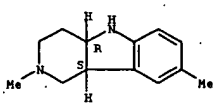
L9 ANSWER 37 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:238901 CA
TITLE: Ion-pair extraction of [3H]stobadine from biological fluids
AUTHOR(S): Scasnar, V.
CORPORATE SOURCE: Institute Experimental Pharmacology, Slovak Academy Sciences, Bratislava, 84216, Slovakia
SOURCE: Journal of Radioanalytical and Nuclear Chemistry (1998), 228(1-2), 99-104
CODEN: JRNCDM; ISSN: 0236-5731
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple and specific radiometric assay was developed for the determination of stobadine, a cardioprotective drug, in blood serum of exptl. animals. The assay is based on a single extraction step of the radioactively labeled drug from serum into the benzene solution of dicarbolide of cobalt followed by quantitation of the extracted radioactivity by liquid scintillation counting. The extraction mechanism involves the ion-pair formation between the protonized mol. of stobadine and the hydrophobic, neg. charged mol. of dicarbolide of cobalt. The extraction yield of stobadine from 1 mL of serum was 95% in the concentration range from 1 to 6000 ng/mL. The co-extraction of metabolites was <5%. The method was applied to the determination of stobadine in serum of dogs and the data obtained were in a good agreement with those obtained by high performance liquid chromatog.

IT 95751-51-2, Stobadine dihydrochloride
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ion-pair extraction of [3H]stobadine from biol. fluids)

RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



●2 HCl

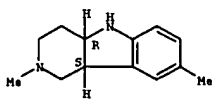
L9 ANSWER 38 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:123776 CA
TITLE: High-molecular-weight hyaluronan - a valuable tool in testing the antioxidative activity of amphiphilic drugs stobadine and vinpocetine
AUTHOR(S): Orvisky, E.; Soltes, L.; Stancikova, Maria
CORPORATE SOURCE: Research Institute of Rheumatic Diseases, Piest'any, SK-92101, Slovakia
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1997), 16(3), 419-424
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antioxidative activity of stobadine and vinpocetine was studied in vitro by measuring their inhibition effect on the depolymn. of the high-mol.-weight hyaluronan by hydroxyl radicals. The radicals were generated by the Cu2+ - H2O2 system. Hyaluronan depolymn. was monitored by size exclusion chromatog. The antioxidative activity of stobadine and vinpocetine was compared to that of D-mannitol. A 50% inhibition of hyaluronan depolymn. was reached at stobadine and vinpocetine concns. of 1.7+10-6 and 3.0+10-7 mol l-1, resp., while a D-mannitol level of 2.6+10-3 mol l-1 was needed to achieve the same inhibitory effect.

IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-mol.-weight hyaluronan in testing of antioxidative activity of amphiphilic drugs stobadine and vinpocetine)

RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

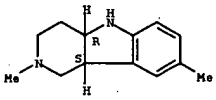
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 39 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:112503 CA
TITLE: Effective one/two step purification of various materials by solid-phase extraction
AUTHOR(S): Soltes, Ladislav; Sabille, Bernard
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-842 16, Slovakia
SOURCE: Biomedical Chromatography (1997), 11(6), 348-351
CODEN: BICHE2; ISSN: 0269-3879
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Simple one/two step purification procedures based on the solid-phase extraction technique were effectively exploited to clean up radiolabeled drugs represented by dihydrochloride of [6-3H]-stobadine and hydrochloride of [4-3H]-pentacaine, derivatization agents such as 4-nitrobenzoyl chloride or 3,5-dinitrobenzoyl chloride, as well as the aqueous phosphate or triethylamine acetate buffer solns.
IT 85202-17-1P, (-)-Stobadine
RL: PUR (Purification or recovery); PREP (Preparation)
(purification of various materials by solid-phase extraction)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



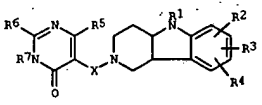
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 40 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:34772 CA
TITLE: Hexahydropyrido[4,3-b]indole derivatives as antipsychotic drugs
INVENTOR(S): Kennis, Ludo Edmond Josephine; Mertens, Josephus Carolus
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

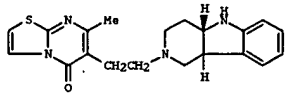
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744040	A1	19971127	WO 1997-EP2710	19970515 <--
W: AL, AM, AU, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, LC, LK, LR, LT, LV, MD, MG, MK, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 470745	B	20020101	TW 1997-86105765	19970501 <--
CA 2254755	AA	19971127	CA 1997-2254755	19970515 <--
AU 9729616	A1	19971209	AU 1997-29616	19970515 <--
AU 714113	B2	19991216		
EP 902684	A1	19990324	EP 1997-924014	19970515 <--
EP 902684	B1	20030409		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				
CN 1219875	A	19990616	CN 1997-194873	19970515 <--
JP 2000510860	T2	20000822	JP 1997-541588	19970515 <--
CZ 287961	B6	20010314	CZ 1998-3774	19970515 <--
AT 236636	E	20030415	AT 1997-924014	19970515
PT 902684	T	20030829	PT 1997-924014	19970515
IL 127177	A1	20031031	IL 1997-127177	19970515
ES 2196332	T3	20031216	ES 1997-924014	19970515
PL 187345	B1	20040630	PL 1997-330079	19970515
ZA 9704470	A	19981123	ZA 1997-4470	19970522 <--
KR 2000005226	A	20000125	KR 1998-707913	19981002 <--
US 6057325	A	20000502	US 1998-180366	19981109 <--
NO 9805389	A	19990120	NO 1998-5389	19981119 <--
NO 311724	B1	20020114		

PRIORITY APPLN. INFO.: EP 1996-201450 A 19960523
WO 1997-EP2710 W 19970515
OTHER SOURCE(S): MARPAT 128:34772
GI

L9 ANSWER 40 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



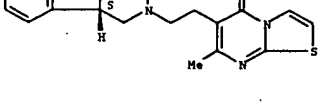
I



II

AB Title compds. I [X = alkanediyl; R1 = H, alkyl, aryl, aralkyl; R2,R3, R4 = H, halo, hydroxy, nitro, cyano, alkyl, alkoxy, trifluoromethyl, alkylthio, mercapto, amino, mono-, dialkylamino, carboxyl, alkyloxycarbonyl, alkylcarbonyl; R5 = H, alkyl, Ph, phenylmalkyl; R6 = H, alkyl, alkoxy, alkylthio, (un)substituted NH2; R7 = H, alkyl; R6R7 = (un)substituted (CH2)3, (CH2)4, CH:CHCH2, CH2CH:CH, CH:CHCH:CH], having central dopamine and serotonin antagonistic activity, were prepared Thus, 2-benzyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole was reduced to the hexahydro analog, debenzylated, and treated with 6-(2-chloroethyl)-7-methyl-5H-thiazolo[3,2-a]pyrimidin-5-one to give the product II. II had dopamine and serotonin antagonistic activity in the combined apomorphine, tryptamine, and norepinephrine test in rats.
IT 199725-48-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hexahydropyrido[4,3-b]indole derivs. as antipsychotic drugs)
RN 199725-48-9 CA
CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-(1,3,4,4a,5,9b-hexahydro-2H-pyrido[4,3-b]indol-2-yl)ethyl]-7-methyl-, trans- (9CI) (CA INDEX NAME)

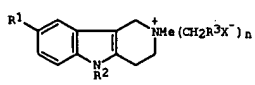
Relative stereochemistry.



L9 ANSWER 41 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 127:248096 CA
TITLE: Preparation of hydrogenatad pyrido[4,3-b]indole derivatives and pharmaceutical compositions and a method for treating neurodegenerative diseases
INVENTOR(S): Zefirov, Nikolai Serafimovich; Afanasiev, Andrei Zakharovich; Afanasieva, Svetlana Vasilievs; Bachurin, Sergei Olegovich; Thachenko, Sergei Evgenievich; Grigoriev, Vladimir Viktrovich; Jurovskaya, Marina Abramovna
PATENT ASSIGNEE(S): Isukura Sangyo K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 156 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09216882	A2	19970819	JP 1996-274909	19961017 <--
RU 2140417	C1	19991027	RU 1995-117585	19951017 <--

PRIORITY APPLN. INFO.: RU 1995-117585 A 19951017
OTHER SOURCE(S): MARPAT 127:248096
GI

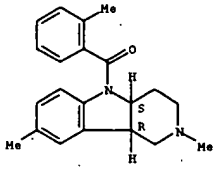


I

AB The title derivs. I [dotted line represents an optional bond; R1 = H, lower alkyl; R2 = 2-[2-(N-methyl-N-R3-methylamino)ethyl]-5-R1-indolyl-3-Me, (CZ)m(CHAlk)l(CH2)kY [Y = H, halo, cycloalkyl, ethenyl which may be substituted with 1-3 lower alkyl, 1 aryl, CO2R4 at the β-position (R4 = H, alkyl, aralkyl, aryl), OR4, alkylsulfonyl, arylsulfonyl, NR5R6 [R5-6 = H, alkyl, cycloalkyl, aralkyl, aryl, 2-, 3-, or 4-pyridyl, alkylsulfonyl, arylsulfonyl; one of R5 and R6 = COR7 (R7 = H, alkyl, alkoxy, cycloalkyl, aralkyl, aryl, 2-, 3-, or 4-pyridyl); or R5R6 = (CH2)2W(CH2)2 [W = O, (CH2)q (q = 0-2), N(CV)rR8 (R8 = H, alkyl, aryl; CV = CH2, CO; r = 0-1)] or NR5R6 = N-phthalimido], OR9 (R9 = H, alkyl, aralkyl, aryl, OH, alkoxy, NR5R6 except N-phthalimido, 2-, 3-, or 4-pyridyl), cyano, CX3 (X = Cl, F, Br), aryl, 2-, 3-, or 4-pyridyl or their quaternary ammonium salt, trialkylammonium, cycloalkylammonium, N-azinium, N-azolium]; CZ = CO, CS, CH2; k = 0-4; l, m, n = 0-1; R3 = (CH2)kY' (Y' = any group given for Y); X = pharmacol. acceptable acid anion] and their pharmacol. acceptable salts are prepared by several methods. Also claimed are a method for treating diseases affecting glutamate neuromediator systems, e.g. neurodegenerative disorders, especially Alzheimer disease, with I and pharmaceutical compns. containing I.
2-Methyl-8-isopropyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole hydrochloride (prepared from 4-isopropylphenylhydrazine hydrochloride and N-methyl-4-piperidone) showed ED50 17 mg/kg against convulsive death of mice induced by injection of NMDA into paracele. Pharmaceutical formulations containing I were also given.
IT 195326-87-5P

L9 ANSWER 41 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of hydrogenated pyrido[4,3-b]indole derivs. as NMDA antagonists for treating neurodegenerative diseases)
RN 195326-87-5 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-5-(2-methylbenzoyl)-, monohydrochloride, cis- (9CI) (CA INDEX NAME)

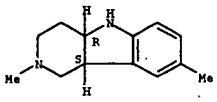
Relative stereochemistry.



● HCl

L9 ANSWER 42 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 127:158506 CA
TITLE: Stobadine pretreatment enhances glutathione peroxidase activity in the heart of irradiated mice
AUTHOR(S): Kovacikova, Zuzana; Chorvatovicova, Darina; Ginter, Emil
CORPORATE SOURCE: Institute of Preventive and Clinical Medicine, Bratislava, Slovakia
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (1997), 19(4), 241-243
CODEN: MFEPDX; ISSN: 0379-0355
PUBLISHER: Prous
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of pretreatment with stobadine (a novel drug with cardioprotective properties) on the activity of glutathione peroxidase was studied in the heart of mice after Co60 irradiation Exposure to 6.5 Gy caused
significant decrease in the activity of the enzyme. Treatment with stobadine (70.07 mg/kg) 1 or 2 h before irradiation resulted in activity enhancement in comparison with the non-pretreated irradiated group. We conclude that the radical scavenging mechanism may be involved in the protection exerted by stobadine. The results are in agreement with those obtained by the micronucleus test.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stobadine pretreatment enhances glutathione peroxidase activity in the heart of irradiated mice)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

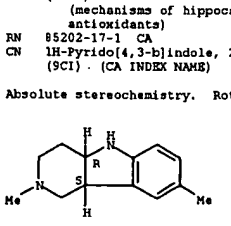
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 43 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:325467 CA
TITLE: Mechanisms of hippocampal reoxygenation injury. Treatment with antioxidants
AUTHOR(S): Horakova, L'.; Stolc, S.; Chromikova, Z.; Pekarova, A.; Derkova, L'.
CORPORATE SOURCE: Inst. Experimental Pharmacol., Slovak Acad. Sci., Bratislava, 842 16, Slovakia
SOURCE: Neuropharmacology (1997), 36(2), 177-184
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of hypoxia of different durations (8, 12 or 15 min) and of subsequent reoxygenation were studied in rat hippocampal slices by measuring enzyme activities related to oxidative stress: superoxide dismutase (SOD), cytochrome c oxidase and lactate dehydrogenase (LDH). Simultaneously the degree of lipid peroxidn. was estimated by measuring conjugated dienes (CD). Reoxygenation after 8-min of hypoxia induced general cell injury indicated by increased LDH activity. Reoxygenation after 12-min of hypoxia started lipid peroxida. assessed by an increase in CD, and after 15-min of hypoxia followed by reoxygenation CD were found to be significantly decreased, suggesting lipid degradation The injury induced by a hypoxia of 12 min and reoxygenation was reduced by SOD and catalase, indicating that oxygen radicals were involved in this process. The oxygen radicals originated from the xanthine/xanthine oxidase system, from the synthesis of prostaglandins, as well as from the mitochondrial respiratory chain, since allopurinol, indomethacin and rotenone decreased while antimycin increased reoxygenation injury. An increase in ATP may also have been involved as cyanide, an inhibitor of ATP synthesis, decreased the reoxygenation injury. The chain-breaking antioxidants trolox, alpha tocopherol and the pyridoindole stobadine were effective in preventing reoxygenation injury, indicating the involvement of lipid peroxidn. in this process.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of hippocampal reoxygenation injury and treatment with antioxidants)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

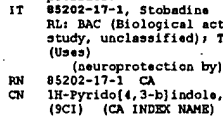
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 44 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:271624 CA
TITLE: Neuroprotection by the pyridoindole stobadine: a minireview
AUTHOR(S): Stolc, S.; Vlkolinsky, R.; Pavlasek, J.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-842 16, Slovakia
SOURCE: Brain Research Bulletin (1997), 42(5), 335-340
CODEN: BRBUDU; ISSN: 0361-9230
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 55 refs., summarizing data documenting that stobadine (STB) may protect nerve structures against oxidative stress. This was demonstrated by the impairment of synaptic transmission in hippocampal slices and sympathetic ganglia exposed to hypoxia/reoxygenation (H/R) in vitro as well as by survival of rats and dogs exposed to brain ischemia/reperfusion (I/R) in vivo. The STB effect was linked mostly to its free-radical-scavenging and antioxidant properties. STB seems to act primarily on phospholipids, thus protecting the integrity and function of somatic membranes in neurons as well as those in subcellular organelles, such as mitochondria and endoplasmic reticulum. STB prevented damage to Ca2+-sequestering systems in endoplasmic reticulum and synaptosomes induced by lipid-peroxidn. initiators. STB diminished changes in NMDA and adrenergic α1-receptors evoked in the brain by I/R or H/R. It prevented the decrease in brain total thiols, participating in tissue antioxidative protection, under these conditions. It readily penetrates into both the hydrophilic and the hydrophobic compartments of the central nervous system. In I/R, protection of structures such as cerebral blood vessels, endothelium, and/or erythrocytes may participate in the effect of STB, besides the direct protection of nervous tissue. STB may be a potential protectant of the central nervous system in diseases in which oxidative injury may play an important role, i.e., stroke, neurotrauma, chronic brain ischemia, or some neurodegenerative diseases. It could provide a useful model in the further search for novel compds. with even more pertinent pharmacol. and pharmacokinetic profiles.
IT 85202-17-1, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotection by)
RN 85202-17-1 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



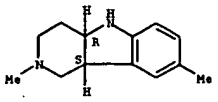
L9 ANSWER 45 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:233312 CA
TITLE: Effect of long-term administration of stobadine on exploratory behavior and on striatal levels of dopamine and serotonin in rats and their offspring
AUTHOR(S): Dubovicky, M.; Ujhazy, E.; Kovacovsky, P.; Rychlik, I.; Kalnovicova, T.; Navarova, J.; Turcani, P.; Durisova, M.; Gajdosik, A.
CORPORATE SOURCE: Inst. Experimental Pharmacol., Bratislava, Slovakia
SOURCE: Journal of Applied Toxicology (1997), 17(1), 63-70
CODEN: JJATDK; ISSN: 0260-437X
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Stobadine (STB), a cardioprotective drug, was evaluated for its effect on the intensity and habituation of exploratory behavior in open field testing and on the levels of striatal dopamine (DA), serotonin (5-HT) and their metabolites (3,4-dihydroxyphenylacetic acid, homovanillic acid, 5-hydroxyindole-3-acetic acid) in rats and their offspring. Dams were treated by oral gavage with STB (50 mg kg-1) for a total of 56 days from 14 days before mating to day 21 postpartum (pp). The first open field measurements of the dams were performed over 4 days at the beginning of the experiment, the second on days 21-24 pp and the third on days 49-52 pp (recovery period). Their offspring were tested on postnatal (pn) days 30-33 and 60-63. The biochem. anal. (HPLC with electrochem. detection) in the dams was performed at the same time schedule as given for the open field testing, but in their offspring only on pn day 60. Motor activity of the dams was decreased on days 21-24 pp. The increase of motor activity in female offspring was observed on pn days 30-33. Neurochem. anal. of the striatum of the dams revealed a significant increase of the levels of DA, 5-HT and 5-hydroxyindole-3-acetic acid. In male offspring the levels of DA were significantly decreased, whereas in females the levels were increased. These results suggest that maternal administration of STB resulted both in dams and their offspring in minor alterations in spontaneous behavior components and changes in the dopaminergic and serotonergic system, but without inducing overtly detectable toxicity.
IT 85202-18-2, DP 1031
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of long-term administration of stobadine on exploratory behavior and on striatal levels of dopamine and serotonin in rats and their offspring)
RN 85202-18-2 CA
CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 85202-17-1
CMF C13 H18 N2

Absolute stereochemistry. Rotation (-).

L9 ANSWER 45 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



CM 2

CRN 57-10-3
CMF C16 H32 O2

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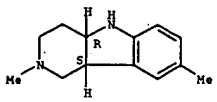
L9 ANSWER 46 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:796 CA
TITLE: Effect of long-term administration of stobadine to rats on selective variables of spontaneous behavior of their offspring
AUTHOR(S): Dubovicky, M.; Kovacovsky, P.; Rychlik, I.; Ujhazy, E.; Gajdosik, A.
CORPORATE SOURCE: Institute Experimental Pharmacology, Slovak Academy Sciences, Bratislava, 82416, Slovakia
SOURCE: General Physiology and Biophysics (1996), 15(2), 181-186
CODEN: GPBIE2; ISSN: 0231-5882
PUBLISHER: Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigated the effect of long-term administration of the cardioprotective drug stobadine (STB) to dams on selective variables of spontaneous behavior of their offspring in open field (horizontal and vertical activities, frequency and duration of grooming, and duration of total activity and immobility) tested on day 60 of age. The treatment of dams with STB significantly increased horizontal activity of offspring in both sexes. The other variables studied were not affected, with the exception of a significant increase in the frequency and duration of grooming and in the duration of total activity in females compared to males from STB treated dams.
IT 95751-51-2, Stobadine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(effect of long-term administration of stobadine to rats on selective variables of spontaneous behavior of their offspring)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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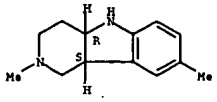
L9 ANSWER 47 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 125:185795 CA
TITLE: Transport of an antihypoxic drug stobadine across the blood-brain barrier in rat striatum and its influence on catecholamine-oxidative current: A voltammetric study under normal and anoxic/ischemic conditions
AUTHOR(S): Pavlasek, J.; Haburcak, M.; Masanova, C.; Stolc, S.
CORPORATE SOURCE: Institute Normal and Pathological Physiology, Slovak Academy Sciences, Bratislava, Slovakia
SOURCE: Physiological Research (Prague) (1996), 45(3), 193-204
CODEN: PHRSEJ; ISSN: 0862-8408
PUBLISHER: Academia
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Differential pulse voltammetry with a carbon fiber microelectrode (ME) was used in pentobarbital-anesthetized rats for monitoring the stobadine current (STB.C) on both sides of the blood-brain barrier (BBB) in the arterial bloodstream (BS) and in the corpus striatum (CS). The STB.C exhibited a distinct peak at a polarization voltage 540±30 mV. The maximum of STB.C in BS attained 2-3 min after the STB administration (2.8 mg/100 g in 1.0 mL saline solution i.a.) was followed by a rapid decrease to about 20% within next 3 min. The STB readily passed across the BBB: the STB.C peak appeared in the CS in the 3rd minute and continued to rise up to the 30th min. The administration of STB did not prevent a large increase (1347±326 %) of the catechol-oxidative current (CA.OC) occurring in the CS between the 4th and 5th minute after cardiac arrest. However, a decrease of ME sensitivity to CA.OC in the presence of STB was observed. This fact leads to the speculation whether a similar "quenching" of dopamine by STB could not participate in the protective effects of STB observed in the brain exposed to hypoxia-reoxygenation.
IT 95751-51-2, Stobadine
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(transport of an antihypoxic drug stobadine across the blood-brain barrier in rat striatum and its influence on catecholamine-oxidative current)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

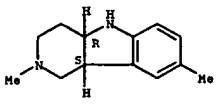


●2 HCl

L9 ANSWER 48 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 125:76265 CA
TITLE: Rabbit brain endoplasmic reticulum membranes as target for free radicals. Changes in Ca2+-transport and protection by stobadine
AUTHOR(S): Racay, Peter; Kaplan, Peter; Lehotsky, Jan; Mezesova, Viera
CORPORATE SOURCE: Comenius Univ., Dep. Biochem., Martin, SK-036 01, Slovakia
SOURCE: Biochemistry and Molecular Biology International (1995), 36(3), 569-577
CODEN: BMBIES; ISSN: 1039-9712
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Incubation of rabbi brain endoplasmic reticulum membranes with either ferrous sulfate/EDTA or ferrous sulfate/EDTA and hydrogen peroxide led to the loss of efficiency of membranes to sequester Ca2+, which did not correlate with changes in conjugated diene formation. The production of practically non-detectable amount of conjugated dienes that occurs during the period of incubation of microsomes with lipid peroxidn. initiators represents lipid peroxidn. that is enough to produce changes in membrane permeability towards Ca2+. Addition of stobadine was able to prevent Ca2+ transport damage in a dose-dependent manner and drug concns. higher than 200 μM were able in the authors model system to confer the defense against free radical and heavy metal initiated lipid peroxidn. The EC50 values for microsomes with Fe2+ and Fe2+/H2O2 were 12 μM and 25 μM, resp. In the authors model system, stobadine seems to be at least as effective as butylated hydroxytoluene, which is considered to be a good chain-breaking antioxidant. In contrast to stobadine, α-tocopherol acetate was less potent, the effect of 1 mM α-tocopherol acetate being comparable to the effect of 20 μM stobadine.
IT 95751-51-2, Stobadine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rabbit brain endoplasmic reticulum membranes as target for free radicals determined by lipid peroxidn. in relation to changes in Ca2+-transport and protection by antioxidant stobadine)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L9 ANSWER 48 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



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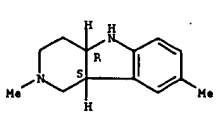
L9 ANSWER 49 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 125:3697 CA
TITLE: The pyridoindole antioxidant stobadine inhibited glycation-induced absorbance and fluorescence changes in albumin
AUTHOR(S): Stefek, M.; Drozdikova, I.; Vajdova, K.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia
SOURCE: Acta Diabetologica (1996), 33(1), 35-40
CODEN: ACDAEZ; ISSN: 0940-5429
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied the effect of the pyridoindole antioxidant stobadine on glycation-induced absorbance and fluorescence changes in bovine serum albumin (BSA), used as a model protein. Incubation of BSA (4 mg/mL) with glucose (100-400 mM) in 0.12 M phosphate buffer, pH 7.4, in the presence of 100 μM Cu2+ at 37° resulted in a time-dependent increase of absorbance (320 nm) and fluorescence (excitation 350 nm, emission 415 nm). The process was found to be dependent on the presence of oxygen and transition metal ions, but equimolar iron could not fully substitute for the activity of copper. The glucose-induced chromo- and fluorophore formation was reduced significantly by stobadine. For 200 mM glucose, in 7- and 14-day incubations, 51%-60% inhibition was obtained at a stobadine concentration of 0.1 mM, and the effect leveled off at higher concns. of the drug. No inhibition was observed with N-acetyl stobadine, a derivative with restricted antioxidant activity. Since stobadine did not affect the Amadori product formation determined by the thiobarbituric acid (TBA) method as 5-hydroxymethyl furfural (5-HMF) released in boiling oxalic acid, the inhibitory action of stobadine may be explained by its interference with metal-catalyzed oxidation reactions following after the glycation step. The results obtained suggest that antioxidant therapy could be used to limit the damage from adverse glycation-induced processes in diabetes mellitus.
IT 95751-51-2, Stobadine
RL: BAC (Biological activity or effector, except adverse); EPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pyridoindole antioxidant stobadine inhibited glycation-induced absorbance and fluorescence changes in albumin)
RN 95751-51-2 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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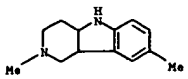
L9 ANSWER 50 OF 134 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 124:332651 CA
TITLE: Simultaneous monitoring of dopamine, its metabolites and trans-isomer of atypical neuroleptic drug carbidine concentrations in striatal dialyzates of conscious rats
AUTHOR(S): Gainetdinov, Raul R.; Sotnikova, Tatyana D.; Grekhova, Tatyana V.; Rayevsky, Kirill S.
CORPORATE SOURCE: Institute Pharmacology, Russian Academy Medical Sciences, Moscow, Russia
SOURCE: Progress in Neuro-Psychopharmacology & Biological Psychiatry (1996), 20(2), 291-305
CODEN: PNPPD7; ISSN: 0278-5846
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1.Transcerebral microdialysis was used to monitor dopamine, 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA) and trans-isomer of atypical neuroleptic drug carbidine concns. in the dialyzates from dorsal striatum of freely moving rats following i.p. administration of the drug at doses 0.5, 1, 5 and 25 mg/kg. The changes in locomotor activity as well as catalepsy in rats following trans-carbidine administration were also evaluated. 2.The microdialysis "point of no net flux" method was used to measure interstitial free concentration (IFC) of trans-carbidine in the dorsal striatum of freely moving rats following i.p. administration of the drug at dose 5 mg/kg. The maximal IFC of trans-carbidine was found to be approx. 1 μM 20-40 min after injection. 3.The drug at doses up to 1 mg/kg produces elevation of dopamine release not affecting sufficiently its metabolite dialyzate levels. IFC of the drug calculated for these doses will not exceed 0.24 μM. At the dose 5 mg/kg, i.p., elevation of both dopamine release and metabolism was observed and dopamine release increased slightly more than DOPAC dialyzate levels. 4.Stimulatory action of trans-carbidine on locomotor activity of non-operated rats has been observed at doses 0.2 and 0.5 mg/kg, i.p. 5.Only the dose 25 mg/kg of trans-carbidine (maximal calculated IFC 4.53 μM) was found to be cataleptogenic. The drug at this dose failed to increase DA release but induced a marked increase of DOPAC and HVA output. 6.It is concluded that trans-carbidine in in vivo neurochem. and behavioral studies demonstrates the preferential antagonistic action on dopamine release-regulating autoreceptors.
IT 33162-17-3, Carbidine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(simultaneous monitoring of dopamine, metabolites and trans-isomer of atypical neuroleptic drug carbidine concns. in striatal dialyzates of conscious rats)
RN 33162-17-3 CA
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride (8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 50 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



●2 HCl

10/743,449

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L3         1026 S L1 FULL

     FILE 'CA' ENTERED AT 14:49:03 ON 13 JUL 2005
L4          315 S L3
L5         2702 S 5HT
L6            1 S L4 AND L5
L7          149 S L4 AND (PHARM? OR DRUG?)
L8          150 S L6 OR L7
L9          134 S L7 AND PY<2003

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STN INTERNATIONAL LOGOFF AT 14:50:42 ON 13 JUL 2005
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